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Ashley

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(54) **METHODS OF TREATING ACNE**(75) Inventor: **Robert A. Ashley**, Newtown, PA (US)(73) Assignee: **Galderma Laboratories, Inc.**, Fort Worth, TX (US)

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(51) **Int. Cl.****A61K 9/68** (2006.01)(52) **U.S. Cl.** **424/401; 514/152**(58) **Field of Classification Search** None
See application file for complete search history.(56) **References Cited**

U.S. PATENT DOCUMENTS

4,704,383 A	11/1987	McNamara et al.
5,122,519 A	6/1992	Ritter
5,260,292 A *	11/1993	Robinson et al. 514/198
5,674,539 A	10/1997	Tomas et al.
5,827,840 A	10/1998	Ramamurthy et al.
5,908,838 A	6/1999	Gans
5,998,390 A	12/1999	Ramamurthy et al.
6,455,583 B1 *	9/2002	Pflugfelder et al. 514/528
6,673,843 B2	1/2004	Arbiser
7,014,858 B2	3/2006	Ashley
2003/0082120 A1	5/2003	Milstein
2003/0148945 A1	8/2003	McNicol et al.
2005/0239723 A1	10/2005	Amin et al.

FOREIGN PATENT DOCUMENTS

EP	0 410 099 A1	1/1991
WO	WO 83/00628	3/1983
WO	WO 99/58131	11/1999

OTHER PUBLICATIONS

Akamatsu, et al. "Effect of Keigai-Rengyo-To, a Japanese Kampo Medicine, on Neutrophil Functions: a Possible Mechanism of Action of Keigai-Rengyo-To in Acne," *The Journal of International Medical Research*, 25: 255-265 (1997).

Baer, et al. "High-Dose Tetracycline Therapy in Severe Acne," *Arch Dermatol*, 112:479-481 (Apr. 1976).

Cheryl Guttman, "Emerging resistance changes face of antibiotic therapy for acne," *Dermatology Times*, Jan. 2001, p. 22.

Hirohiko Akamatsu, Maki Asada, Jinro Komura, Yasuo Asada, and Yukie Niwa, "Effect of Doxycycline on the Generation of Reactive Oxygen Species: A Possible Mechanism of Action of Acne Therapy with Doxycycline," *Acta Derm Venereol (Stockh)* 72:178-178 (1992). Bodokh, Y. Jacomet, J. Ph. Lacour and J.P. Ortonne, "Minocycline Induces an Increase in the Number of Excreting Pilosebaceous Follicles in Acne Vulgaris," *Acta Derm Venereol (Stockh)*, 77:255-259 (1997).

W. J. Cunliffe, M.D., F.R.C.P., "Evolution of a Strategy for the Treatment of Acne," *J Am Acad Dermatol*, 16:591-9 (1987).

E. Anne Eady, Eileen Ingham, Christina E. Walters, Jonathan H. Cove, and William J. Cunliffe, "Modulation of Comedonal Levels of Interleukin-1 in Acne Patients Treated with Tetracyclines," *J. Invest Dermatol*, 101:86-91 (1993).

Boni E. Elewski, M.D., Beth A.J. Lamb, W. Mitchell Sams, Jr., M.D., and W. Ray Gammon, M.D., "In Vivo Suppression of Neutrophil Chemotaxis by Systemically and Topically Administered Tetracycline," *J Am Acad Dermatol*, 8:807-812 (1983).

Nancy B. Esterly, M.D., Nancy L. Furey, M.D., and Lillian E. Flanagan, B.S., "The Effect of Antimicrobial Agents on Leukocyte Chemotaxis," *The Journal of Investigative Dermatology*, 70(1):51-55 (1978).

Sainte-Marie, I. Tenaud, O. Jumbou and B. Dréno, "Minocycline Modulation of Alpha-MSH Production by Keratinocytes In vitro," *Acta Derm Venereol* 79:265-267 (1999).

Hoshiki Miyachi, M.D., Akira Yoshioka, M.D., Sadao Imamura, M.D., and Yukie Niwa, M.D., "Effect of Antibiotics on the Generation of Reactive Oxygen Species," *J Invest Dermatol*, 86(4):449-453 (1986).

Gerd Plewig, M.D., and Erwin Schöpf, M.D., "Anti-Inflammatory Effects of Antimicrobial Agents: An In Vivo Study," *The Journal of Investigative Dermatology*, 65:532-536 (1975).

M. Toyoda and M. Morohashi, "An Overview of Topical Antibiotics for Acne Treatment," *Dermatology*, 196:130-134 (1998).

Sheila E. Unkles, and Curtis G. Gemmell, "Effect of Clindamycin, Erythromycin, Lincomycin, and Tetracycline on Growth and Extracellular Lipase Production by Propionibacteria In Vitro," *Antimicrobial Agents and Chemotherapy*, 21:39-43 (1982).

G.F. Webster, K.J. McGinley, and J.J. Leyden, "Inhibition of Lipase Production in *Propionibacterium acnes* by Sub-Minimal-Inhibitory Concentrations of Tetracycline and Erythromycin," *British Journal of Dermatology*, 104:453-457 (1981).

Guy F. Webster, M.D., Ph.D., Susan M. Toso, M.S., and Lutz Hegemann, M.D., "Inhibition of a Model of In Vitro Granuloma Formation by Tetracyclines and Ciprofloxacin," *Arch Dermatol.*, 130:748-752 (1994).

Reynold C. Wong, M.D., Sewon Kang, M.P.H., Jan L. Heezen, L.P. N., John J. Voorhees, M.D., and Charles N. Ellis, M.D., "Oral Ibuprofen and Tetracycline for the Treatment of Acne Vulgaris," *J Am Acad Dermatol*, 11:1076-1081 (1984).

Kenneth S. Kornman and Edward H. Karl, "The Effect of Long-Term Low-Dose Tetracycline Therapy on the Subgingival Microflora in Refractory Adult Periodontitis," *J. Periodontol.*, 53(10):604-610 (Oct. 1982).

(Continued)

Primary Examiner — Susan Tran

(74) *Attorney, Agent, or Firm* — Hoffman & Baron, LLP

(57) **ABSTRACT**

A method of treating acne in a human in need thereof comprising administering systemically to said human a tetracycline compound in an amount that is effective to treat acne but has substantially no antibiotic activity, without administering a bisphosphonate compound.